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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,750	03/22/2005	In-San Kim	428.1050	8168

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EXAMINER

ARNOLD, ERNST V

ART UNIT	PAPER NUMBER
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1616

DATE MAILED: 07/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/528,750	KIM ET AL.	
	Examiner	Art Unit	
	Ernst V. Arnold	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 March 2005 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>3/22/05</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

The Examiner acknowledges receipt of application number 10/528,750 filed on 03/22/2005, which is a 371 of PCT/KR02/01837 filed on 09/30/2002.

Claims 1-10 are pending.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Hansson et al. (WO 96/02259).

Hansson et al. disclose the use of chitosan and a polysaccharide for the manufacture of an agent capable of providing stimulated regeneration of hard tissue such as bone tissue (Claims 1 and 2). Hansson et al. disclose a composition made by adding an aqueous solution of 2% w/v chitosan to a solution of dextran sulphate or heparin or chondroitin-4-sulphate (0.1 w/v) in tripolyphosphate buffer (Page 11, example 12). Hansson et al. disclose that the resulting beads were positioned subperiostally on the frontal bone of adult rats and bone formation was assessed after 3 weeks (Page 11, lines 23-26). Hansson et al. disclose that the beads are osteogenic and that even better stimulation of healing can be achieved by combining the invention with growth factors

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and experiments were performed with acidic Fibroblast Growth Factor (FGF) (Page 11, line 28-page 12, line 9).

Claim Rejections - 35 USC § 102

Claims 1, 2, and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Shu et al. (International Journal of Pharmaceutics 2000, 201, 51-58).

Shu et al. disclose a tripolyphosphate/chitosan complex beads for controlled release drug delivery (Abstract). Shu et al. disclose the addition of model drugs to the beads and it is therefore the Examiner's position that composition of Shu et al. could additively contain a material for stimulation bone-formation and bone-consolidation (Abstract). Shu et al. disclose a composition that is 4% chitosan and 1% tripolyphosphate, which the Examiner interprets to read upon instant claim 4 Page 52, right column last paragraph).

With respect to the art rejection above, it is noted that the reference does not teach that the composition can be used in the manner instantly claimed, stimulating bone-formation and bone-consolidation, however, the intended use of the claimed composition does not patentably distinguish the composition, per se, since such undisclosed use is inherent in the reference composition. In order to be limiting, the intended use must create a structural difference between the claimed composition and the prior art composition. In the instant case, the intended use does not create a structural difference, thus the intended use is not limiting.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hansson et al. (WO 96/02259) in view of Kim et al. (Journal of Cellular Biochemistry 2000, 77, 169-178) and Shu et al. (International Journal of Pharmaceutics 2000, 201, 51-58) and Santos et al. (US 5,955,096) and Wilson et al. (Development 1997, 124, 3177-3184).

Applicant claims: A composition containing tripolyphosphate and water-soluble chitosan for stimulating bone-formation and bone-consolidation.

Determination of the scope and content of the prior art

(MPEP 2141.01)

The reference of Hansson et al. and Shu et al. are discussed in detail above and that discussion is hereby incorporated by reference.

Kim et al. teach the administration of 50 $\mu\text{g/ml}$ and 100 $\mu\text{g/ml}$ of $\beta\text{ig-h3}$ on osteoblast differentiation (Page 174, left column and page 175, Figure 5).

Santos et al. teaches drug delivery systems and that chitosan microspheres can be prepared by dissolving the polymer in acidic solution and crosslinking it with tripolyphosphate (Abstract; and column 11, lines 63-65). Santos et al. teach the drugs that can be delivered with these systems include growth factors such as FGF, PDGF, EGF and TGF-beta (Column 14, lines 15-33).

Wilson et al. teach the administration of various concentrations of bone morphogenetic protein 4 from 1 ng/ml to 100 ng/ml (Pages 3179-3180, Figures 1-3).

**Ascertainment of the difference between the prior art and the claims
(MPEP 2141.02)**

1. Hansson et al. do not expressly teach the composition for stimulating bone-formation and bone-consolidation as set forth in claim 2, wherein the material for stimulating bone-formation and bone-consolidation is selected from a group consisting of $\beta\text{ig-h3}$, bone morphogenic protein, TGF- β , IGF-I and PDGF.

2. Hansson et al. do not expressly teach the composition for stimulating bone-formation and bone-consolidation wherein the ratio of tripolyphosphate to water-soluble chitosan is 20:80 - 80:20 weight% or 50:50 weight %..

3. Hansson et al. do not expressly teach the composition for stimulating bone-formation and bone-consolidation wherein the $\beta\text{ig-h3}$ is added at the concentration of 100 $\mu\text{g/ml}$ - 1 $\mu\text{g/ml}$ or 300 $\mu\text{g/ml}$ - 600 $\mu\text{g/ml}$.

4. Hansson et al. do not expressly teach the composition for stimulating bone-formation and bone-consolidation wherein the bone morphogenic protein is added at the concentration of 50 ng/ml - 500 ng/ml or 100 ng/ml - 300 ng/ml or is BMP-4.

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

1 and 4. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the composition of Hansson et al. with a material for stimulating bone-formation and bone-consolidation selected from a group consisting of β ig-h3, bone morphogenic protein, TGF- β , IGF-I and PDGF, as suggested by Santos et al. and Wilson et al., and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Hansson et al. disclose that the beads are osteogenic and that even better stimulation of healing can be achieved by combining the invention with growth factors. One of ordinary skill in the art would then have been motivated to add osteogenic agents to the composition of Hansson et al. with the expectation of success and would have looked for guidance in the amount of agents to use from Wilson et al.

2. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to make the composition of Hansson et al. in a 50:50; or 20:80 to 80:20 tripolyphosphate to water soluble chitosan weight % because Shu et al. teach 4% chitosan and 1% tripolyphosphate. The adjustment of particular working conditions (e.g., the different weight ratios of tripolyphosphate to water soluble chitosan)

is deemed merely a matter of routine optimization, which is within the ability of one of ordinary skill in the art.

One of ordinary skill in the art would have been motivated to do this because Shu et al. teach this range for drug delivery and modification of the ratio of ingredients is expected to produce drug delivery vehicles of different properties. One of ordinary skill in the art would want the best drug delivery vehicle for their application and would be inclined to experiment with different ratios of ingredients to develop that vehicle.

3. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to add β ig-h3 at the concentration of 100 μ g/ml - 1 μ g/ml or 300 μ g/ml - 600 μ g/ml, as suggested by Kim et al., to the composition of Hansson et al. and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Hansson et al. teach the addition of growth factors and Kim et al. teach the administration of 50 μ g/ml and 100 μ g/ml of β ig-h3 on osteoblast differentiation. One of ordinary skill in the art would have added this amount of β ig-h3 to the composition of Hansson et al. and produced the instant invention. The adjustment of particular working conditions (e.g., adding more β ig-h3 to the composition of Hansson et al.) is deemed merely a matter of routine optimization, which is within the ability of one of ordinary skill in the art.

In the absence of any criticality/unexpected results, the presently claimed invention is considered prima facie obvious over the prior art for the reasons of record and those stated above.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976).

A prior art disclosure is not limited to its working examples or to its preferred embodiments. (*Merck & Co. Inc. v. Biocraft Labs. Inc.*, 874 F.2d 804, 807, 10 USPQ2d 1843, 1846 (Fed. Cir. 1989); *In re Fracalossi* 681 F.2d 792, 794 n. 1, 215 USPQ 569, 570 n.1 (CCPA 1982); *In re Lamberti*, 545 F.2d 747, 750, 192 USPQ 278, 280 (CCPA 1976); *In re Boe*, 355 F.2d 961, 965, 148 USPQ 507, 510 (CCPA 1996).

Accordingly, the burden of proof is upon Applicants to show that the instantly claimed subject matter is different and unobvious over those taught by the prior art. (See: *In re Brown*, 173 USPQ 685, 688; *In re Best*, 195 USPQ 430 and *In re Marosi*, 218 USPQ 289, 293).

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

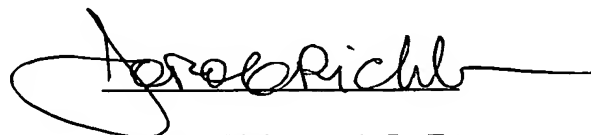
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ernst V. Arnold whose telephone number is 571-272-8509. The examiner can normally be reached on M-F (6:15 am-3:45 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ernst Arnold
Patent Examiner
Technology Center 1600
Art Unit 1616

A handwritten signature in black ink, appearing to read 'J. Richter', with a large, sweeping loop at the beginning and end.

Johann Richter, Ph.D. Esq.
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